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The value of forced expiratory volume in 1 s in screening subjects with stable COPD for PaO_2 <7·3 kPa qualifying for long-term oxygen therapy

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Guidelines on the management of chronic obstructive pulmonary disease (COPD) issued by the European Respiratory Society (ERS), British Thoracic Society (BTS), American Thoracic Society (ATS), and Department of Health for England and Wales (DoH) suggest differing values of forced expiratory volume in 1 s (FEV_1) below which arterial blood gas analysis should be performed to determine the presence of severe hypoxaemia and possible long-term oxygen therapy (LTOT) requirement. This study aimed to determine the value of FEV_1 at these different levels in screening for LTOT requirement defined as PaO_2 <7·3 kPa in subjects with stable COPD. Comparative measures were taken against other lung function tests of volume and diffusing capacity. A retrospective analysis of paired lung function and arterial oxygen measurements in 491 subjects was made. The positive and negative predictive values, sensitivity and specificity of FEV_1 <70% predicted (ERS), FEV_1 <50% predicted (ATS), FEV_1 <40% predicted (BTS) and FEV_1 <1·5 l (DoH) were determined for fulfilling LTOT criteria (PaO_2 <7·3 kPa). The correlation between lung function variables and PaO_2 was established. Logistic regression analysis was used to classify subjects with PaO_2 <7·3 kPa and PaO_2 ⩾7·3 kPa.

Using FEV_1 to screen for LTOT requirement produced a high negative predictive value at all four suggested limits (FEV_1 <70% 100%, FEV_1 <50% 96%, FEV_1 <40% 95%, FEV_1 <1·5 l 97%). However, the positive predictive values were low (FEV_1 <70% 13%, FEV_1 <50% 16%, FEV_1 <40% 19%, FEV_1 <1·5 l 15%) as were sensitivities. No single lung function variable was a strong determinant of PaO_2. FEV_1 % pred (r=0·40), FVC % pred (r=0·34) and TLCO % pred (r=0·27) had the strongest relationships. Logistic regression also placed FEV_1 % pred and TLCO % pred as the best predictors of PaO_2 <7·3 kPa. We conclude no lung function variable correlates well with PaO_2 in subjects with stable COPD. The best predictor of PaO_2 <7·3 kPa was FEV_1 % pred. Whilst a low FEV_1 is a poor predictor of LTOT requirement in an individual, PaO_2 <7·3 kPa is only found in subjects with a low FEV_1. A high FEV_1 may be used to exclude subjects from further investigation for LTOT and prevent unnecessary arterial sampling.

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Introduction

Domiciliary oxygen used for a minimum of 15 h day^{-1} may extend the life expectancy of subjects with severe hypoxaemic chronic obstructive pulmonary disease (COPD) (1,2). The indications for prescription in the U.K. are based upon arterial blood gas values of PaO_2 <7·3 kPa, although PaO_2 <8 kPa in subjects with documented salt and water retention is a further indication in many centres. The Department of Health England and Wales (DoH) Drugs Tariff (3) recommends screening using spirometry followed by arterial blood gas analysis (ABG). This provides confirmation of airflow obstruction and may reduce the need for universal blood gas analysis. Spirometric values are also used to classify severity of COPD in the management guidelines issued by the American Thoracic Society (ATS) (4), European Respiratory Society (ERS) (5), and most recently the British Thoracic Society (BTS) (6). The need to consider oxygen therapy and hence arterial blood gas analysis is based upon spirometrically defined severity in these guidelines although different levels of FEV_1 are suggested in each document. The European guidelines specifically state that the relationship between spirometry and arterial oxygenation is poor but do not reference this and recommend oxygen therapy be considered in all cases of COPD. We determined to establish the relationship between FEV_1 and arterial oxygen levels in a large number of subjects with stable COPD and to assess the value of using the various

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suggested screening levels of FEV_1 in identifying patients likely to benefit from LTOT.

Subjects and Methods

We retrospectively analysed the lung function data collected in the Department of Medicine at Charing Cross Hospital over a 9-year period from 634 subjects with diagnostic coding for COPD. All subjects were coded for diagnosis by their referring doctor at the time of testing. A 10% sample of cases was analysed to categorize the seniority of the referring doctor in order to validate the accuracy of the coding. Sixty-eight percent were of specialist consultant grade, 24% of registrar status and the remainder at more junior level.

Details of hospital number, age, sex, height, weight, haemoglobin, and smoking history were retrieved from the hospital mainframe computer system. Lung function tests of spirometry, lung volumes determined by multibreath helium dilution, and diffusing capacity determined by single breath helium dilution and corrected for haemoglobin, were performed on all subjects and recorded as absolute values and as percent of their predicted mean values (% pred) (7). The lung function equipment used was either the PK Morgan Transfer Test Mark I (PK Morgan, Gillingham, U.K.) or the Gould CPI 500IV (Sensor Medics, Rugby, U.K.). Validation of the two separate systems has previously been made (8) and between-system reproducibility shown to be similar to that of intra-system reproducibility.

Arterial blood gas samples were taken from the radial or brachial artery using a heparinized syringe by medical staff. Analysis was carried out using the Corning 168 pH/Blood gas analyser (Ciba Corning, Halstead) or the ABL300 Acid-base Laboratory (Radiometer, Copenhagen).

The data were then transferred to a PC and analysed using SPSSPC for Windows (SPSS inc. Chicago, U.S.A.). An initial data search was performed to eliminate transcription errors. Subjects with an FEV_1 >80% predicted or whose FEV_1/FVC ratio was not reduced (i.e. >70% predicted) were eliminated as not fulfilling the criteria for COPD, 92 subjects in all. This was to exclude smokers with symptoms but without significant airflow obstruction. Those who fulfilled the criteria but who had demonstrated >15% reversibility on bronchodilator testing, 51 subjects, were also excluded from the study, i.e. asthmatic responders. A further case note sample of 10% of the remaining subjects was examined to confirm the clinical diagnosis which was agreed as COPD in each case sampled. No subjects were tested when acutely unwell.

Descriptive statistics were performed comprising mean, median, range and SD. The four FEV_1 screening criteria suggested by the DoH, ATS, ERS, and BTS, to assess for PaO_2 <7·3 kPa were then applied to the subject group and their sensitivity, specificity, positive and negative predictive powers calculated.

Correlation coefficients were then calculated for all the measured lung function variables with PaO_2 and scatterplots examined.

Univariate logistic regression analysis applied to all the measured lung function variables was then used to classify subjects into two groups with PaO_2 values either below 7·3 kPa or equal to or greater than 7·3 kPa.

Results

Of the original 634 subjects there were 491 who satisfied the criteria for COPD and who had complete data sets for analysis. There were 347 males. Ages ranged from 41 to 90 years, mean 66·2 (9·2), height range 1·42 m–1·92 m, mean 1·67 (0·09), and body mass index range 15·4–42·8, mean 24·2 (4·7). Mean (SD) values and ranges for lung function data are given in Table 1. Fifty of the 491 subjects had a PaO_2 <7·3 kPa.

Sensitivity, specificity, positive and negative predictive values using the various FEV_1 screening criteria to selected subjects with PaO_2 <7·3 kPa are shown in Table 2.

Correlation coefficients for all lung function variables with PaO_2 expressed both in absolute measurements and as percent of predicted values (% pred) are shown in Table 3. The statistical significance of logistic regression analysis used for each individual lung function variable to classify subjects into those with PaO_2 greater than or equal to or less than 7·3 kPa are also given in the same table. The relative risk (RR) values describe the risk per unit value of the individual variable in classifying the study subjects correctly into the two groups PaO_2 less than 7·3 kPa or equal to or more than 7·3 kPa. Whilst none of the values have high correlation coefficients or logistic regression sensitivity, FEV_1 is shown to be superior to all the other parameters tested.

The correlations between FEV_1 % pred with PaO_2 are shown as a scatterplot in Fig. 1.

Discussion

This study has defined the value and limitations of the use of the FEV_1 as a screening tool in the detection of severe hypoxaemia defined as a PaO_2 <7·3 kPa, in a large number of subjects with stable COPD. An FEV_1 above the screening levels suggested by the guidelines referenced has a high negative predictive value and in the absence of clinical signs suggesting otherwise virtually excludes severe hypoxaemia requiring LTOT. In contrast an FEV_1 below the suggested screening level has a poor predictive value for severe hypoxaemia and cannot be used to identify LTOT requirement (Table 2).

The level of FEV_1 set to determine screening for ABG does affect the positive and negative predictive value of the test as well as the sensitivity and specificity. Raising the level of FEV_1 increases the negative predictive value but produces a reduction in the positive predictive value although all these changes were relatively small applied to the data set in this study (Table 2). The effect on sensitivity as applied to screening the COPD population is more marked (Table 2). Those using FEV_1 either as a determinant of severe hypoxia in an individual or in screening a

TABLE 1. Descriptive statistical data for lung function variables and anthropomorphic measures in 491 subjects with stable COPD

	Mean	STDDEV	Minimum	Maximum
Age (years)	66·2	9·2	41	90
Height (m)	1·66	0·09	1·43	1·89
BMI	24·2	4·7	15·4	42·8
FEV_1 (l)	1·10	0·51	0·20	2·75
FEV_1 (% pred)	(42·1)	(15·9)	(8·6)	(79·5)
FVC (l)	2·42	0·87	0·45	5·46
FVC (% pred)	(73·0)	(19·0)	(12·3)	(133·1)
FEF_{50} (l)	0·43	0·11	0·19	0·64
RV (l)	3·41	0·98	1·18	6·84
RV (% pred)	(140·1)	(54·5)	(59·0)	(329·2)
TLC (l)	6·17	1·43	3·19	10·02
TLC (l) (% pred)	(97·2)	(17·3)	(48·0)	(161·3)
TLCO (mmol min^{-1} kPa^{-1})	4·84	1·92	0·68	12·88
TLCO (% pred)	(56·9)	(21·9)	(11)	(144)
TLCO/VA (mmol min^{-1} kPa^{-1} l^{-1})	1·12	0·38	0·20	2·32
TLCO/VA (% pred)	(61·3)	(24·9)	(13)	(142)
PaO_2 (kPa)	9·19	1·44	5·57	12·97
$PaCO_2$ (kPa)	5·55	0·82	3·03	8·32

population group must be aware of these effects when setting limits which should be adjusted according to the requirements of the user.

There are limitations to this study. The findings presented here may not be universally applicable and should be used in similar population groups, i.e. stable COPD patients sufficiently compromised to warrant referral to hospital. Second, our analysis was retrospective and some sampling error is inevitable. The diagnostic code entered by the clinician at the time of testing cannot be verified in every case but a 10% sample of subjects revealed that 92% had been coded as COPD by medical staff with specialist respiratory training. Further attempts were made to eliminate miscoding errors by ensuring all subjects fulfilled spirometric criteria for COPD and excluding those with reversible airflow obstruction. The strength of the data base is in the large number of subjects studied which should minimize the impact of a small number of individual inaccuracies.

When considering the relationship of lung function variables with PaO_2 the measure of lung function that best correlates with PaO_2 and predicts PaO_2 <7·3 kPa appears to be the FEV_1 % pred (r=0·40) which demonstrated minimal advantage over the FEV_1 expressed in absolute terms (r=0·39). It has a considerable advantage over all other measurements (Table 3).

TABLE 2. Sensitivity, specificity, positive and negative predictive powers of the levels of FEV_1 recommended as screening tests for PaO_2 <7·3 kPa

FEV_1	Sensitivity	Specificity	PPV	NPV
<1·5 l	95%	23%	15%	97%
<40% pred	80%	52%	19%	95%
<50% pred	91%	32%	16%	96%
<70% pred	100%	7%	13%	100%

Correlations demonstrated for FEV_1 and FVC with arterial oxygen are similar to those recorded in previous studies of smaller numbers of subjects with COPD (9–13). Correlations were slightly improved using % predicted rather than absolute measures in our study. Although this might seem logical it contrasts with some previous smaller studies (9,10,12) where absolute terms had slightly better correlates than when expressed as % predicted. The differences are not great however and the larger sample size of the current study may have produced a more significant statistical result on that basis alone.

These findings of relatively low correlations and poor specificity are not too surprising interpreted in the light of the currently postulated mechanisms of hypoxia in COPD (alveolar hypoventilation, impaired alveolar-end capillary diffusion, increased vascular shunt, ventilation/perfusion (V/Q) mismatching, (14). Mismatching is thought to be the dominant factor in stable COPD (14–17). Small airway obstruction and partial blockage of larger airways by mucous impaction contribute significantly to V/Q inequality. The FEV_1 is predominantly influenced by the large airways and may not accurately reflect important pathophysiological changes in the smaller airways. In addition the FEV_1 has no diagnostic ability to reflect abnormalities in pulmonary perfusion which may contribute to ventilation–perfusion mismatch. Alternative techniques such as pulse oximetry combined with lung function tests may improve the screening value but this method when considered alone also has significant limitations (18).

TABLE 3. Correlation coefficients for association between lung function variables expressed both in absolute measurements and percent of predicted mean values with measured PaO_2. Relative risks (RR) and confidence intervals (CI) of logistic regression in classification of subjects into those with PaO_2 <7·3 kPa or ≥7·3 kPa

Variable	Correlation coefficient (Spearman)	Significance	Logistic regression RR	CI		*P* value
Age (years)	−0·3	n.s.	1·014	0·98,	1·048	n.s.
FEV_1 (l)	0·39	<0·0001	6·380	2·58,	15·80	0·0001
FEV_1 (% pred)	0·40	<0·0001	1·058	1·03,	1·09	<0·0001
FVC (l)	0·33	<0·0001	1·876	1·267,	2·778	0·0017
FVC (% pred)	0·34	<0·0001	1·030	1·011,	1·049	0·0016
RV (l)	−0·07	n.s.	1·180	0·88,	1·58	n.s.
RV (% pred)	0·01	n.s.	0·997	0·991,	1·003	n.s.
TLC (l)	0·11	0·043	1·290	1·03,	1·60	0·0237
TLC % pred	0·13	0·014	1·014	0·997,	1·032	n.s.
TLCO (mmol min^{-1} kPa^{-1})	0·25	<0·0001	1·470	1·21,	1·78	0·0001
TLCO % pred	0·27	<0·0001	1·041	1·022,	1·060	<0·0001
TLCO/VA (mmol min^{-1} kPa^{-1} l^{-1})	0·06	n.s.	2·350	1·07,	5·16	0·0327
TLCO/VA % pred	0·09	n.s.	1·021	1·007,	1·035	0·0034

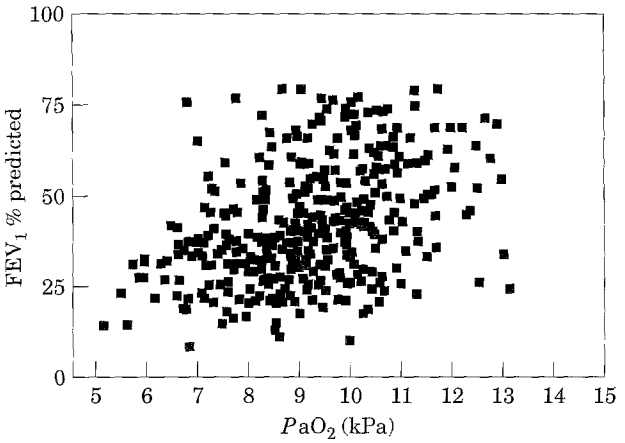

FIG. 1. Scattergram showing correlation of FEV_1 predicted with PaO_2.

Clinical signs of salt and water retention may also alert the clinician to the probability of cor pulmonale in a subject with a low FEV_1.

In summary none of the measured lung function variables are good predictors of severe hypoxaemia. FEV_1 is probably the best single test when expressed as % predicted and is easily performed. When applied to an individual with a value above those suggested for screening it has a high negative predictive power which should reduce referrals for unnecessary arterial sampling. Subjects with lower values of FEV_1 will still require arterial blood gas analysis.

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